

IN THE SPECIFICATION

Replace paragraph [0013] with the following  
rewritten paragraph [0013] and [0013.1]:

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[0013] c-Raf (SEQ ID NO:1); Araf (SEQ ID NO:2); Braf (SEQ ID NO:3); cyclic AMP dependent protein kinases a, b and g (cAPK) (SEQ ID NO:4 to 5); protein kinase C alpha through theta (PKC) (SEQ ID NO:6 to 12); Akt 1 and 2 (also called Rac  $\alpha$  and  $\beta$ ) (SEQ ID NO:13); glycogen synthase kinase  $\alpha$  and  $\beta$  (GSK3) (SEQ ID NO:14 to 15); casein kinases type II  $\alpha$  and  $\alpha'$  (CK) (SEQ ID NO:16 to 17); G-receptor coupled protein kinase  $\beta$ -2 adrenergic receptor kinases 1 and 2 (bARK1, 2) (SEQ ID NO:18); G-protein coupled receptor kinases GRK1 and GRK4 through GRK6 (SEQ ID NO:19 to 22); calmodulin dependent kinases types I and II a, b, c and d (CaMK) (SEQ ID NO:23 to 24); members of the Polo-associated family: Plk, Plx1, polo, SNK, CDC5, Sak, Prk, Fnk, Plo1 (SEQ ID NO:25 to 32); MARK1 and MARK2 and p78 (SEQ ID NO:33 to 34); cyclin dependent kinases 2, 4 and 6 (SEQ ID NO:35 to 37); Src, Yes, Fyn, Fgr, Lyn, Hck, Lck (SEQ ID NO:38 to 44); Csk and Matk (SEQ ID NO:45 to 46); focal adhesion kinase (FAK) (SEQ ID NO:47); c-Abl (SEQ ID NO:48); endothelial growth factor receptors Tie, Tek, FGF receptor (Flg, Bek, FGFR3, FGFR4), PDGF receptor  $\alpha$  and  $\beta$ , Flt 1 and 4 and Flk1 (SEQ ID NO:49 to 59); HGF receptors c-Met, c-Sea and Ron (SEQ ID NO:60 to 62); EGF receptor (EGFR, ErbB2,

Q1 ErbB3, ErbB4) (SEQ ID NO:63 to 66); Ret (SEQ ID NO:67); NGF receptors (Trk) (SEQ ID NO:68 to 70); Syk and Zap70 (SEQ ID NO:71 to 72); Jak kinases 1 through 3 and Tyk2 (SEQ ID NO:73 to 76); Iak1 (SEQ ID NO:77); Chk1 (SEQ ID NO:78); NFkB inhibitor kinases, known also as I-kappa B kinases IKK1 and IKK2 (SEQ ID NO:79 to 80); death associated protein kinase (DAPK) (SEQ ID NO:81); insulin receptor kinase (IRK) (SEQ ID NO:82); ~~TGF $\alpha$~~  TGF $\beta$  receptor type II (SEQ ID NO:83); Activin receptor type II A and B (ACTR) (SEQ ID NO:84 to 85); Activin receptor-like kinases 1 through 6 (ALK1, 2, 3, 4, 5, 6) (SEQ ID NO:86 to 90); discoidin domain receptor 1 (DDR) and Tyro10 (SEQ ID NO:91 to 92); ILK (SEQ ID NO:93); Jun kinase (JNK) (SEQ ID NO:94).

[0013.1] Figures 2A-2F are a group of sequences illustrating the consensus amino acid sequences of the  $\alpha$ D region found among the family of protein kinases. Also shown are examples of conservative substitutions in these amino acid sequences. The Conservative amino acid substitutions shown include the amino acid sequences of the  $\alpha$ D region of: c-Raf (SEQ ID NO:1); Araf (SEQ ID NO:2); Braf (SEQ ID NO:3); cyclic AMP dependent protein kinases a, b and g (cAPK) (SEQ ID NO:4 to 5); protein kinase C alpha through theta (PKC) (SEQ ID NO:6 to 12); Akt I and 2 (also called Rae  $\alpha$  and  $\beta$ ) (SEQ ID NO:13); glycogen synthase kinase  $\alpha$  and  $\beta$  (GSK3) (SEQ ID NO:14 to 15);

casein kinases type 11  $\alpha$  and  $\alpha'$  (CK) (SEQ ID NO:16 to 17); G-receptor coupled protein kinases P-2 $\beta$ -2 adrenergic receptor kinases 1 and 2 (bARK1, 2) (SEQ ID NO:18); G-protein coupled receptor kinases GRK1 and GRK4 through GRK6 (SEQ ID NO:19 to 22); calmodulin dependent kinases types I and II a, b, c and d (CaMK) (SEQ ID NO:23 to 24); members of the Polo-associated family: Plk, Plxl, polo, SNK, CDC5, Sak, Prk, Fnk, Plol (SEQ ID NO:25 to 32); NLkRK1 and MARK2 and p78 (SEQ ID NO:33 to 34); cyclin dependent kinases 2, 4 and 6 (SEQ ID NO:35 to 37); Src, Yes, Fyn, Fgr, Lyn, Hck, Lck (SEQ ID NO:38 to 44); Csk and Matk (SEQ ID NO:45 to 46); focal adhesion kinase (FAK) (SEQ ID NO:47); c-Abl (SEQ ID NO:48); endothelial growth factor receptors Tie, Tek, FGF receptor (Flg, Bek, FGFR3, FGFR4), PDGF receptor  $\alpha$  and  $\beta$ , Flt 1 and 4 and Flk1 (SEQ ID NO:49 to 59); HGF receptors c-Met, cSea and Ron (SEQ ID NO:60 to 62); EGF receptor (EGFR, ErbB2, ErbB3, ErbB4) (SEQ ID NO:63 to 66); Ret (SEQ ID NO:67); NGF receptors (Trk) (SEQ ID NO:68 to 70); Syk and Zap70 (SEQ ID NO:71 to 72); Jak kinases 1 through 3 and Tyk2 (SEQ ID NO:73 to 76); I $\kappa$ B (SEQ ID NO:77); Chk1 (SEQ ID NO:78); NF $\kappa$ B inhibitor kinases IKK1 and IKK2 (SEQ ID NO:79 to 80); death associated protein kinase (DAPK) (SEQ ID NO:81); insulin receptor kinase (IRK) (SEQ ID NO:82); ~~TGFP~~ TGF $\beta$  receptor type II (SEQ ID NO:83); Activin receptor type 11 A and B (ACTR) (SEQ ID NO:84 to 85); Activin receptor-like

Q1 kinases 1 through 6 (ALK1, 2, 3, 4, 5, 6) (SEQ ID NO:86 to 90); discoidin domain receptor 1 (DDR) and Tyro 10 (SEQ ID NO:91 to 92); ILK (SEQ ID NO:93); and Jun kinase (JNK) (SEQ ID NO:94). An "\*" indicates an aliphatic, substituted aliphatic, benzylic, substituted benzylic, aromatic or substituted aromatic ester of glutamic acid or aspartic acid.

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Replace paragraph [0043] with the following rewritten paragraph [0043]:

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Q2 [0043] Examples of PKs whose activity can be modulated by peptide and peptide derivatives, as described herein, include, but are not limited to, PKs belonging to the following PK families: polo family (Glover et al., *J. Cell Biol.*, 135:1681 (1996)), Raf (Pritchard et al., *Nat. Genet.* 16:214 (Jul 1997)), mitogen-activated protein kinases (MAP kinases), Akt/PKB (Frank et al., *Cell* 88:435 (1997) and Hemmings et al., *Science* 275:628 (1997)), G protein-coupled receptor kinases (Premont et al., *FASEB J.* 9:175 (Feb 1995)), Casein kinases, HGF receptors (Boros, *The Lancet* 345:293 (Feb 1995)), Cyclin-Dependent kinases, PDGF receptors, NGF receptors, Jak kinases, NFkB inhibitor kinases (Maniatis, *Science* 278:818 (Oct 1997)), Activin receptors, ~~TGF $\beta$~~ -TGF $\beta$  receptors, Discoidin domain receptors (Vogel et al., *Molec. Cell. Biol.* 1:13 (Dec 1997)), Src, EGF-R, FGF-R, VEGF-R, HGF-R, PDGF-R, the insulin receptor family and the neurotrophin

Q2 receptor family. Suitable members of the Polo family include, but are not limited to, Plk, Plx1, polo, SNK, CDC5, Sak, Prk, Fnk, Plol. Suitable members of the Src family include, but are not limited to, c-Src, c-Yes, FYN, FGR, HCK, LYN, LCK and BLK. Suitable members of the EGF-R family include, but are not limited to EGFR, ErbB2, ErbB3 and ErbB4. Suitable members of the FGF-R family include, but are not limited to FGFR1, FGFR2, FGFR3 and FGFR4. Suitable members of the VEGF-R family include, but are not limited to, Flt1, Flt4 and Flk1. Suitable members of the insulin receptor family include, but are not limited to, INS-R, IRR and IGF1-R. Suitable members of the HGF receptor family include, but are not limited to, c-Met, c-Sea and Ron. Other suitable PKs include, but are not limited to, cyclic AMP (cAMP) dependent protein kinase, protein kinase C, calmodulin dependent kinase, glycogen synthase kinase-3 (GSK3) and cyclic GMP (cGMP) dependent protein kinase, RET (Pasini et al., *TIG* 12(4):138 (Apr 1996)), CSK, Matk, c-Abl, FAK (Frisch et al., *J. Cell. Biol.* 134(3):793 (Aug 1996)), MARK1, 2 and P78 (Drewes et al., *Cell* 89:297 (Apr 1997)), Tie and Tek, Syk and Zap70 (Arpaia et al., *Cell* 76:947 (1994)), Iak1, Chk1 (Sanchez et al., *Science* 277:1497 (Sept 1997)), DAPK, ILK (Hannigan et al., *Nature* 379:91 (Jan 1996)) and JNK.

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Replace paragraph [0044] with the following  
rewritten paragraph [0044]:

[0044] As shown in Figure 1, the sequences of suitable peptide members of the  $\alpha$ D region of PKs from different families include, but are not limited to: c-Raf (SEQ ID NO:1); Araf (SEQ ID NO:2); Braf (SEQ ID NO:3); cyclic AMP dependent protein kinases a, b and g (CAPK) (SEQ ID NO:4 to 5); protein kinase C alpha through theta (PKC) (SEQ ID NO:6 to 12); Akt 1 and 2 (also called Rac  $\alpha$  and  $\beta$ ) (SEQ ID NO:13); glycogen synthase kinase  $\alpha$  and  $\beta$  (GSK3) (SEQ ID NO:14 to 15); casein kinases type II  $\alpha$  and  $\alpha'$  (CK) (SEQ ID NO:16 to 17); G-receptor coupled protein kinases  $\beta$ -2 adrenergic receptor kinases 1 and 2 (bARK1, 2) (SEQ ID NO:18); G-protein coupled receptor kinases GRK1 and GRK4 through GRK6 (SEQ ID NO:19 to 22); calmodulin dependent kinases types I and II a, b, c and d (CaMK) (SEQ ID NO:23 to 24); members of the Polo-associated family: Plk, Plx1, polo, SNK, CDC5, Sak, Prk, Fnk, Plol (SEQ ID NO:25 to 32); MARK1 and MARK2 and p78 (SEQ ID NO:33 to 34); cyclin dependent kinases 2, 4 and 6 (SEQ ID NO:35 to 37); Src, Yes, Fyn, Fgr, Lyn, Hck, Lck (SEQ ID NO:38 to 44); Csk and Matk (SEQ ID NO:45 to 46); focal adhesion kinase (FAK) (SEQ ID NO:47); c-Abl (SEQ ID NO:48); endothelial growth factor receptors Tie, Tek, FGF receptor (Flg, Bek, FGFR3, FGFR4), PDGF receptor  $\alpha$  and  $\beta$ , Flt 1 and 4 and Flk1 (SEQ ID NO:49 to

Q3

Q3 59); HGF receptors c-Met, c-Sea and Ron (SEQ ID NO:60 to 62); EGF receptor (EGFR, ErbB2, ErbB3, ErbB4) (SEQ ID NO:63 to 66); Ret (SEQ ID NO:67); NGF receptors (Trk) (SEQ ID NO:68 to 70); Syk and Zap70 (SEQ ID NO:71 to 72); Jak kinases 1 through 3 and Tyk2 (SEQ ID NO:73 to 76); Iak1 (SEQ ID NO:77); Chk1 (SEQ ID NO:78); NFkB inhibitor kinases IKK1 and IKK2 (SEQ ID NO:79 to 80); death associated protein kinase (DAPK) (SEQ ID NO:81); insulin receptor kinase (IRK) (SEQ ID NO:82); ~~TGF $\alpha$~~  TGF $\beta$  receptor type II (SEQ ID NO:83); Activin receptor type II A and B (ACTR) (SEQ ID NO:84 to 85); Activin receptor-like kinases 1 through 6 (ALK1, 2, 3, 4, 5, 6) (SEQ ID NO:86 to 90); discoidin domain receptor 1 (DDR) and Tyro10 (SEQ ID NO:91 to 92); ILK (SEQ ID NO:93); Jun kinase (JNK) (SEQ ID NO:94).

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Replace paragraph [0047] with the following  
rewritten paragraph [0047]:

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Q4 [0047] The present invention includes peptides having amino acid sequences corresponding to a modified sequence or subsequence of the  $\alpha$ D region of PKs and which modulate the activity of PKs including: Akt1/Raca; ALK1; Braf; c-Abl; c-Met; c-Raf; c-Sea; c-Src; CDK2; CDK4; CDK6; Chk1; CK IIa; Csk; Fak; FGFR-3; Flk1; GSK3b; Hck; Iak1; IKK-1; IKK2; ILK; IRK; Jak1; Jak2; Jak3; Lck; Lyn; MARK1; PDGFR-b;

Q4 PKCb; Plk; Ret; Ron; SNK; Syk; ~~TGFBRII~~ TGFBRII; TrkB; and  
Zap70.

Replace paragraph [0049] with the following  
rewritten paragraph [0049]:

Q5 [0049] c-Raf (SEQ ID NO:1); Araf (SEQ ID NO:2); Braf  
(SEQ ID NO:3); cyclic AMP dependent protein kinases a, b and g  
(cAPK) (SEQ ID NO:4 to 5); protein kinase C alpha through  
theta (PKC) (SEQ ID NO:6 to 12); Akt 1 and 2 (also called Rac  
 $\alpha$  and  $\beta$ ) (SEQ ID NO:13); glycogen synthase kinase  $\alpha$  and  $\beta$   
(GSK3) (SEQ ID NO:14 to 15); casein kinases type II  $\alpha$  and  $\alpha'$   
(CK) (SEQ ID NO:16 to 17); G-receptor coupled protein kinases  
 $\beta$ -2 ~~-2~~ adrenergic receptor kinases 1 and 2 (bARK1, 2) (SEQ ID  
NO:18); G-protein coupled receptor kinases GRK1 and GRK4  
through GRK6 (SEQ ID NO:19 to 22); calmodulin dependent  
kinases types I and II a, b, c and d (CaMK) (SEQ ID NO:23 to  
24); members of the Polo-associated family: Plk, Plx1, polo,  
SNK, CDC5, Sak, Prk, Fnk, Plol (SEQ ID NO:25 to 32); MARK1 and  
MARK2 and p78 (SEQ ID NO:33 to 34); cyclin dependent kinases  
2, 4 and 6 (SEQ ID NO:35 to 37); Src, Yes, Fyn, Fgr, Lyn, Hck,  
Lck (SEQ ID NO:38 to 44); Csk and Matk (SEQ ID NO:45 to 46);  
focal adhesion kinase (FAK) (SEQ ID NO:47); c-Abl (SEQ ID  
NO:48); endothelial growth factor receptors Tie, Tek, FGF  
receptor (Flg, Bek, FGFR3, FGFR4), PDGF receptor  $\alpha$  and  $\beta$  Flt 1  
and 4 and Flk1 (SEQ ID NO:49 to 59); HGF receptors c-Met, c-

Q5 Sea and Ron (SEQ ID NO:60 to 62); EGF receptor (EGFR, ErbB2, ErbB3, ErbB4) (SEQ ID NO:63 to 66); Ret (SEQ ID NO:67); NGF receptors (Trk) (SEQ ID NO:68 to 70); Syk and Zap70 (SEQ ID NO:71 to 72); Jak kinases 1 through 3 and Tyk2 (SEQ ID NO:73 to 76); Iak1 (SEQ ID NO:77); Chk1 (SEQ ID NO:78); NFkB inhibitor kinases IKK1 and IKK2 (SEQ ID NO:79 to 80); death associated protein kinase (DAPK) (SEQ ID NO:81); insulin receptor kinase (IRK) (SEQ ID NO:82); ~~TGF $\alpha$~~  TGF $\beta$  receptor type II (SEQ ID NO:83); Activin receptor type II A and B (ACTR) (SEQ ID NO:84 to 85); Activin receptor-like kinases 1 through 6 (ALK1, 2, 3, 4, 5, 6) (SEQ ID NO:86 to 90); discoidin domain receptor 1 (DDR) and Tyro10 (SEQ ID NO:91 to 92); ILK (SEQ ID NO:93); Jun kinase (JNK) (SEQ ID NO:94). The conservative substitutions can occur by exchanging amino acids with aligned  $\alpha$ D region sequences, as shown in Figs. 2A-2F, as well as by substituting the listed amino acids that are not associated with a known  $\alpha$ D region sequence.

Replace paragraph [0050] with the following  
rewritten paragraph [0050]:

Q6 [0050] Specific examples of peptide derivatives of the present invention include peptides: Akt1/Raca K014D001; ALK1 K048D101; Braf K003D001 K003D101; c-Abl K061D101; c-Met K073D101; c-Raf K001D101 K001D001; c-Sea K074D101; c-Src K051D101 K051D001; CDK2 K049D101 K049D001; CDK4 K050D001

Q6 K050D101; CDK6 K089D101; Chk1 K088D102 K088D101; CK II $\alpha$   
K022D001 K022D101; Csk K058D101 K058D001; Fak K060D101; FGFR-3  
K071D101 K071D001 K071D102 K071D901; Flk1 K068D102 K068D101  
K068D001 K068d901; GSK3 $\beta$  K018D003 K018D002 K018D101 K018D001;  
Hck K056D101; Iak1 K087D101; IKK-1 K090D101; IKK2 K091D101;  
ILK K107D101 K107D901; IRK K094D001 K094D101 K094D102 K094D103  
K094D104; Jak1 K084D101K084D102; Jak2 K085D102 K085D105; Jak3  
K086D101 K086D102 K086D103; Lck K057D001 K057D101; Lyn  
K055D101; MARK1 K045D101; PDGFR-b K064D001 K064D101; PKC $\beta$   
K008D101 K008D001; Plk K035D001 K035D101 K035D102; Ret  
K080D101 K080D001; Ron K075D101; SNK K038D101; Syk K082D101;  
~~TGF $\alpha$ RII~~ TGF $\beta$ RII K093D101; TrkB K102D101 K102D106 K102D107  
K102D108 K102D109; Zap70 K083D101 (SEQ ID NO:95 to 170,  
respectively), as specified in Fig . 3A-3D.

Replace paragraph [0052] with the following  
rewritten paragraph [0052]:

Q7 [0052] Also included are peptides having the  
sequence of: Akt1/Raca K014D001; ALK1 K048D101; Braf K003D001  
K003D101; c-Abl K061D101; c-Met K073D101; c-Raf K001D101  
K001D001; c-Sea K074D101; c-Src K051D101 K051D001; CDK2  
K049D101 K049D001; CDK4 K050D001 K050D101; CDK6 K089D101; Chk1  
K088D102 K088D101; CK II $\alpha$  K022D001 K022D101; Csk K058D101  
K058D001; Fak K060D101; FGFR-3 K071D101 K071D001 K071D102  
K071D901; Flk1 K068D102 K068D101 K068D001 K068d901; GSK3 $\beta$

Q7 K018D003 K018D002 K018D101 K018D001; Hck K056D101; Iak1  
K087D101; IKK-1 K090D101; IKK2 K091D101; ILK K107D101  
K107D901; IRK K094D001 K094D101 K094D102 K094D103 K094D104;  
Jak1 K084D101 K084D102; Jak2 K085D102 K085D105; Jak3 K086D101  
K086D102 K086D103; Lck K057D001 K057D101; Lyn K055D101; MARK1  
K045D101; PDGFR-b K064D001K064D101; PKC $\beta$  K008D101 K008D001;  
Plk K035D001 K035D101 K035D102; Ret K080D101 K080D001; Ron  
K075D101; SNK K038D101; Syk K082D101; ~~TGF $\alpha$ RII~~ TGF $\beta$ RII  
K093D101; TrkB K102D101 K102D106 K102D107 K102D108 K102D109;  
Zap70 K083D101 (SEQ ID NO:95 to 170, respectively), as  
specified in Figs. 3A-3D, with the proviso that any one or two  
of the amino residues in the peptide can vary, being replaced  
by any naturally occurring amino acid or analog thereof.

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